APPENDIX A

CURRICULUM VITAE

Name: Ian Hector FRAZER
Date of Birth: 6th January 1953
Place of Birth: Glasgow, Scotland
Nationality: Australian Citizen

Degrees:
BSc (Hons) Pathology (Edinburgh) 1974
MB ChB (Edinburgh) 1977
MD (Melbourne) 1988 "Humoral Immunity to Liver Antigens in Autoimmune liver disease"

Awards:
BHERT award for Collaborative Research 1999
Australian Biotechnology Award 1999
Centenary Medal 2003, for services to cancer research
John Curtin Medal 2005
CSIRO Eureka Award for Leadership in Science 2005
"The Australian" Australian of the Year 2006
Australian of the Year 2006
Suncorp Queenslander of the Year 2006
Queensland Great Award 2006
Distinguished Fellowship Award, Royal College of Pathologists 2006
William Coley Medal, Cancer Research Institute New York 2006
International Life Award (Sezione Ricerca Scientifica), Rome – January 2007
Florey Medal, Sydney – March 2007
Clunies Ross Award – Melbourne – April 2007
International Achievement Summit Golden Plate award – New York - June 2007
2007 Novartis Prize for Clinical Immunology – August 2007 – Rio de Janeiro
Honorary Professor, Shihezi University
Honorary Professor, Chengdu University

Fellowships:
Royal College of Physicians of Edinburgh 1988
Royal College of Pathologists of Australia 1989
Australian Institute of Company Directors 2002
Australian Academy of Science Technology and Engineering 2003
Australian Academy of Science 2004
Royal Australian College of General Practitioners 2007

Travelling fellowships:
Eleanor Roosevelt Cancer Research Fellow (UICC) 1989
Australian Academy of Sciences Travelling Fellowship 1992
William Rudder Travelling Fellowship (QCF) 1993
Christ's College Cambridge visiting Fellowship 2004

Directorships:
For Profit organisations
Coridon Pty Ltd 2002- date
Implicit Biosciences Pty Ltd 2005- date
Biopharmaceuticals Australia Development Pty Ltd 2007
Not for Profit organsiation
Diabetes Vaccine Development Centre 2003 – date

Cancer Council Australia 2002 – date (currently President)
JDRF Pancreatic Islet Transplant Program 2005 – date

Employment History:

1977	House Officer, Roodlands Hospital, Haddington
1977	House Officer, Eastern General Hospital, Edinburgh
1978	Senior House Officer, Medical Renal Unit, Royal Infirmary, Edinburgh
1979	Senior House Officer, Department of Medicine, Eastern General Hospital, Edinburgh
1980	Registrar, Medical Renal Unit, Royal Infirmary, Edinburgh
1981/85	Senior Research Officer, Walter & Eliza Hall Institute, Melbourne
	Assistant, Department of Medicine, University of Melbourne
	Assistant Physician, Clinical Research Unit, Walter & Eliza Hall Institute
1985/88	Senior Lecturer, Department of Medicine, University of Queensland
1985/99	Director, Division of Clinical Immunology, Princess Alexandra Hospital, Queensland
1989/93	Associate Professor, Department of Medicine, University of Queensland
1994-	Professor, Department of Medicine, University of Queensland
1991-	Director, Centre for Immunology and Cancer Research, University of Queensland

Significant invited lectures:

Date	Location	Organisation	Lecture
October 2007	Brisbane	Prince Charles Hospital Foundation	Woolcock Oration
October 2007	Gold Coast	RANZCOG	Arthur Wilson Memorial Oration
September 2007	Sydney	APEC Business Summit 2007	Panellist in session "Educating our people for the future: population, skills and innovation"
July 07	Perth	University of Western Australia	The Sir Wallace Kyle Oration
July 07	Melbourne	Sir Edward Dunlop Medical Research Foundation	"Recent developments and medical advances in medical research"
April 07	Perth	Raine Medical Research Foundation	Raine Oration
April 07	Melbourne	Clunies Ross Dinner	Keynote Address
March 07	Bangkok	Australian Embassy	Keynote Speaker
March 07	Sydney	Pathology Update 2007	Keynote Speaker – Eva Raik Lecture "Cancer Control in the 21st Century"
November 2006	Brisbane	Australian Healthcare Association Congress	Ron Tindle Oration
October 2006	Brisbane	RACP 49th Annual Scientific Conference	Dr William Arnold Connolly Oration
July 2006	Sydney	Biotech Summit	Key opening address "Leading the charge on Vaccine R&D"
July 2006	Brisbane	Earth Dialogues Conference	"How can we shift away from the short term, insular management to honour our long term responsibilities"
July 2006	Perth	HERDSA Conference	Keynote "How can a Scientist survive in academia in the current economic climate"
June 2006	New York	CRI New York Awards Ceremony	Keynote Talk

Date	Location	Organisation	Lecture
June 2006	Portugal	MSD/SPMSD Symposium at the International Congress on Infectious Diseases	"Immune response and long term protection with quadrivalent HPV vaccine: what we know now and what we will know later"
May 2006	Brisbane	Future Summit 2006	Keynote Address "Australia as a knowledge based economy: earning social credit and a positive balance of trace in the 21st Century Global Village"
2005 December	Washington	ICAAC	Invited speaker
2005 March	Geneva	WHO meeting on HPV Vaccines	Speaker/rapporteur
2004 September	Paris	EUROCONFERENCE Vaccines 3: Frontiers in Vaccine Development	Plenary Speaker
2004 February	Bangalore	Australia- India Biotechnology conference	Keynote lecture
2003 September	Auckland	Australasian Society of Microbiology	Bazeley Oration
2003 April	Los Angeles	Development of Therapeutic Cancer Vaccines	Plenary speaker
2002 November	Washington	Pan American Health Organisation 100th Anniversary meeting	Plenary Speaker
2002 July	Washington	NIH Summit on Papillomavirus Vaccines	Plenary Speaker
2001 December	Canberra	Australasian Society for Immunology	Gordon Ada lecture
2000 October	New York	Cancer Research Institute	Plenary Speaker
1999 November	Buenos Aires	World Colopscopy Conference	Keynote Speaker

In 2006 as Australian of the Year I gave over 50 lectures and addresses within Australia

Life Synopsis:
Ian Frazer is director of the Diamantina Institute of Cancer, Immunology and Metabolic Medicine, a research institute of the University of Queensland at the Princess Alexandra Hospital in Brisbane. He was trained as a renal physician and clinical immunologist in Edinburgh, Scotland before emigrating in 1981 to Melbourne, Australia to continue his clinical training and to pursue studies in viral immunology and autoimmunity at the Walter and Eliza Hall institute of Medical Research with Prof Ian Mackay. In 1985 he moved to Brisbane to take up a teaching post with the University of Queensland, and he now holds a personal chair as head of the Diamantina Institute. This centre which Dr Frazer founded in 1991 as the Centre for Immunology and Cancer Research now employs over 80 researchers and trains about 50 postgraduate students. He is currently president of the Cancer Council Australia. Dr Frazer teaches immunology to undergraduate and graduate students of the University.
Dr Frazer's current laboratory research is focussed on development of immunotherapeutic vaccines for papillomavirus associated cancers, for which he holds research funding from several Australian and US funding bodies, and on understanding the local regulation of vaccine developed immune effector responses

in skin. He is pursuing field trials of delivery of HPV vaccines and other methods of cervical cancer control with colleagues in Nepal and Vanuatu, with assistance from Ausaid and the Australian Cervical Cancer Foundation, and advises the WHO on papillomavirus vaccine deployment.

Commercialisation:

Dr Frazer consults for CSL Ltd, Uniquest and Merck in the field of prophylactic and therapeutic papillomavirus vaccines. He is a member of the Merck global advisory board for HPV vaccines and the Science Alliance Advisory Board of Schering Plough Pty Ltd. He consults on an intermittent basis for several biotechnology companies in Australia and the USA. He is a named inventor on patents relating to HPV prophylactic and therapeutic vaccines licenced to CSL, Merck and GSK, on patents on DNA vaccines and on optimising therapeutic protein expression licenced to Coridon Pty Ltd, and on patents relating to optimising immunotherapy.

Research Funding:

Dr Frazer is the inaugural holder of the Queensland government Smart State premier's fellowship, worth $2.5m over 5 years. Dr Frazer has held continuous research funding from the NHMRC since 1985, mostly relating to papillomaviruses or to tumour immunology. He is currently a joint CI on an NHMRC program grant and a NHMRC/Wellcome program grant, together worth >$2m/year. He also holds competitive project grants from NHMRC, the Queensland Cancer Fund, and the Cancer Research Institute of New York.

Significant contributions to Biomedical Research

Since 1983, Dr Frazer has pursued an interest in development of vaccines to prevent human papillomavirus(HPV) infection and the ~0.5m annual deaths from papillomavirus related human cancers in the cervix and elsewhere. In 1985, with colleagues in Melbourne, he demonstrated, at a time when the association of papillomavirus infection with cervical cancer was still contentious, that papillomavirus infection also contributed to anal precancer, particularly in men with immunosuppression as a result of HIV/AIDS, probably the first confirmed example of the relevance of immune surveillance to control of a virus associated cancer in humans. In 1990, he and his then postdoctoral scientist, Dr Jian Zhou, developed the technology for producing human papillomavirus virus like particles. This technology, licenced through the University of Queensland, is now the basis of vaccines recently brought to market by GSK (Cervarix) and Merck (Gardasil) to prevent cervical cancer. The HPV vaccine is only the second vaccine to be produced using recombinant DNA technology, which was necessary because papillomaviruses could not be grown in cell culture. The development of HPV virus like particles was an early product of the application of comparative genomics, as sequence alignment for the genes for the major capsid proteins of a range of papillomaviruses showed that expression of the major capsid protein of the HPV16 virus from the second initiation codon in eukaryotic cells was likely to induce particle formation where conventional expression strategies had failed. Dr Frazer has also developed therapeutic vaccines for chronic HPV infection, one of which is in Phase 2b clinical trials in China and Brisbane with funding from the Cancer Research Institute of New York and The Wellcome Foundation. Dr Frazer has also developed a technology for improving the immune response to polynucleotide vaccines based on differential preferences for codon usage between cells of different lineages, which has been licenced to Coridon Pty Ltd and is currently being used to develop polynucleotide vaccines for Herpesviruses.

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APPENDIX B:

AA= amino acid, CU= codon usage, mc= mammalian consensus, wt= wild-type, onc= oncogenic, non-onc= non-oncogenic, Sec seq= secretory sequence, N/A= not applicable

Summary of Secretory E7 Construct Series 1 and 2

Construct	Amino acid & Codon	Codon usage of Secretory Sequence	Codon usage of E7	E7 Protein
Control Constructs				
IgkC1	N/A	wt	wt	non-onc
IgkC2	N/A	mc	mc	non-onc
IgkC3	N/A	wt	wt	onc
IgkC4	N/A	mc	mc	onc
Secretory E7 construct series 1				
IgkS1-1	Ala GCG	wt	wt with all Ala gcg	non-onc
IgkS1-2	Ala GCA	wt	wt with all Ala gca	non-onc
IgkS1-3	Ala GCT	wt	wt with all Ala gct	non-onc
IgkS1-4	Ala GCC	wt	wt with all Ala gcc	non-onc
IgkS1-5	Arg AGG	wt	wt with all Arg agg	non-onc
IgkS1-6	Arg AGA	wt	wt with all Arg aga	non-onc
IgkS1-7	Arg CGG	wt	wt with all Arg cgg	non-onc
IgkS1-8	Arg CGA	wt	wt with all Arg cga	non-onc
IgkS1-9	Arg CGT	wt	wt with all Arg	non-onc

Construct	Amino acid & Codon	Codon usage of Secretory Sequence	Codon usage of E7	E7 Protein
IgkS1-10	Arg CGC	wt	cgt wt with all Arg cgc	non-onc
IgkS1-11	Asn AAT	wt	wt with all Asn aat	non-onc
lgkS1-12	Asn AAC	wt	wt with all Asn aac	non-onc
lgkS1-13	Asp GAT	wt with all Asp gat	wt with all Asp gat	non-onc
lgkS1-14	Asp GAC	wt with all Asp gac	wt with all Asp gac	non-onc
lgkS1-15	Cys TGT	wt	wt with all Cys tgt	non-onc
lgkS1-16	Cys TGC	wt	wt with all Cys tgc	non-onc
lgkS1-17	Glu GAG	wt with all Glu gag	wt with all Glu gag	non-onc
lgkS1-18	Glu GAA	wt with all Glu gaa	wt with all Glu gaa	non-onc
IgkS1-19	Gln CAG	wt	wt with all Gln cag	non-onc
lgkS1-20	Gln CAA	wt	wt with all Gln caa	non-onc
lgkS1-21	Gly GGG	wt with all Gly ggg	wt with all Gly ggg	non-onc
IgkS1-22	Gly GGA	wt with all Gly gga	wt with all Gly gga	non-onc
IgkS1-23	Gly GGT	wt with all Gly ggt	wt with all Gly ggt	non-onc
IgkS1-24	Gly GGC	wt with all Gly ggc	wt with all Gly ggc	non-onc

Construct	Amino acid & Codon	Codon usage of Secretory Sequence	Codon usage of E7	E7 Protein
IgkS1-25	His CAT	wt	wt with all His cat	non-onc
IgkS1-26	His CAC	wt	wt with all His cac	non-onc
IgkS1-27	Ile ATA	wt	wt with all Ile ata	non-onc
IgkS1-28	Ile ATT	wt	wt with all Ile att	non-onc
IgkS1-29	Ile ATC	wt	wt with all Ile atc	non-onc
IgkS1-30	Lys AAG	wt	wt with all Lys aag	non-onc
IgkS1-31	Lys AAA	wt	wt with all Lys aaa	non-onc
IgkS1-32	Phe TTT	wt	wt with all Phe ttt	non-onc L15F, L22F
IgkS1-33	Phe TTC	wt	wt with all Phe ttc	non-onc L15F, L22F
IgkS1-34	Ser AGT	wt with all Ser agt	wt with all Ser agt	non-onc
IgkS1-35	Ser AGC	wt with all Ser agc	wt with all Ser agc	non-onc
IgkS1-36	Ser TCG	wt with all Ser tcg	wt with all Ser tcg	non-onc
IgkS1-37	Ser TCA	wt with all Ser tca	wt with all Ser tca	non-onc
IgkS1-38	Ser TCT	wt with all Ser tct	wt with all Ser tct	non-onc
IgkS1-39	Ser TCC	wt	wt with all Ser tcc	non-onc
IgkS1-40	Thr ACG	wt with all Thr	wt with all Thr	non-onc

Construct	Amino acid & Codon	Codon usage of Secretory Sequence	Codon usage of E7	E7 Protein
		acg	acg	
IgkS1-41	Thr ACA	wt with all Thr aca	wt with all Thr aca	non-onc
IgkS1-42	Thr ACT	wt with all Thr act	wt with all Thr act	non-onc
IgkS1-43	Thr ACC	wt with all Thr acc	wt with all Thr acc	non-onc
IgkS1-44	Tyr TAT	wt	wt with all Tyr tat	non-onc
IgkS1-45	Tyr TAC	wt	wt with all Tyr tac	non-onc
IgkS1-46	Val GTG	wt with all Val gtg	wt with all Val gtg	non-onc
IgkS1-47	Val GTA	wt with all Val gta	wt with all Val gta	non-onc
IgkS1-48	Val GTT	wt with all Val gtt	wt with all Val gtt	non-onc
IgkS1-49	Val GTC	wt with all Val gtc	wt with all Val gtc	non-onc
IgkS1-50	Leu CTG	altered with Leu ctg	altered with Leu ctg	onc
IgkS1-51	Leu CTA	altered with Leu cta	altered with Leu cta	onc
IgkS1-52	Leu CTT	altered with Leu ctt	altered with Leu ctt	onc
IgkS1-53	Leu CTC	altered with Leu ctc	altered with Leu ctc	onc
IgkS1-54	Leu TTG	altered with Leu ttg	altered with Leu ttg	onc
IgkS1-55	Leu TTA	altered with Leu tta	altered with Leu tta	onc

Construct	Amino acid & Codon	Codon usage of Secretory Sequence	Codon usage of E7	E7 Protein
IgkS1-56	Pro CCG	altered with Pro ccg	altered with Pro ccg	onc
IgkS1-57	Pro CCA	altered with Pro cca	altered with Pro cca	onc
IgkS1-58	Pro CCT	altered with Pro cct	altered with Pro cct	onc
IgkS1-59	Pro CCC	altered with Pro ccc	altered with Pro ccc	onc
Secretory E7 construct series 2				
IgkS2-1	Ala GCG	mc	mc	linkerA-onc
IgkS2-2	Ala GCA	mc	mc	linkerA-onc
IgkS2-3	Ala GCT	mc	mc	linkerA-onc
IgkS2-4	Ala GCC	mc	mc	linkerA-onc
IgkS2-5	Arg AGG	mc	mc	linkerR-onc
IgkS2-6	Arg AGA	mc	mc	linkerR-onc
IgkS2-7	Arg CGG	mc	mc	linkerR-onc
IgkS2-8	Arg CGA	mc	mc	linkerR-onc
IgkS2-9	Arg CGT	mc	mc	linkerR-onc
IgkS2-10	Arg CGC	mc	mc	linkerR-onc
IgkS2-11	Asn AAT	mc	mc	linkerN-onc
IgkS2-12	Asn AAC	mc	mc	linkerN-onc
IgkS2-13	Asp GAT	wt with all Asp gat	wt with all Asp gat	onc
IgkS2-14	Asp GAC	wt with all Asp gac	wt with all Asp gac	onc
IgkS2-15	Cys TGT	wt	wt with all Cys tgt	onc
IgkS2-16	Cys TGC	wt	wt with all Cys	onc

Construct	Amino acid & Codon	Codon usage of Secretory Sequence	Codon usage of E7	E7 Protein
			tgc	
IgkS2-17	Glu GAG	wt with all Glu gag	wt with all Glu gag	onc
IgkS2-18	Glu GAA	wt with all Glu gaa	wt with all Glu gaa	onc
IgkS2-19	Gln CAG	wt	wt with all Gln cag	onc
IgkS2-20	Gln CAA	wt	wt with all Gln caa	onc
IgkS2-21	Gly GGG	wt with all Gly ggg	wt with all Gly ggg	onc
IgkS2-22	Gly GGA	wt with all Gly gga	wt with all Gly gga	onc
IgkS2-23	Gly GGT	wt with all Gly ggt	wt with all Gly ggt	onc
IgkS2-24	Gly GGC	wt with all Gly ggc	wt with all Gly ggc	onc
IgkS2-25	His CAT	mc	mc	linkerH-onc
IgkS2-26	His CAC	mc	mc	linkerH-onc
IgkS2-27	Ile ATA	wt	wt with all Ile ata	onc
IgkS2-28	Ile ATT	wt	wt with all Ile att	onc
IgkS2-29	Ile ATC	wt	wt with all Ile atc	onc
IgkS2-30	Lys AAG	mc	mc	linkerK-onc
IgkS2-31	Lys AAA	mc	mc	linkerK-onc
IgkS2-32	Phe TTT	mc	mc	linkerF-onc
IgkS2-33	Phe TTC	mc	mc	linkerF-onc

Construct	Amino acid & Codon	Codon usage of Secretory Sequence	Codon usage of E7	E7 Protein
IgkS2-34	Ser AGT	wt with all Ser agt	wt with all Ser agt	onc
IgkS2-35	Ser AGC	wt with all Ser agc	wt with all Ser agc	onc
IgkS2-36	Ser TCG	wt with all Ser tcg	wt with all Ser tcg	onc
IgkS2-37	Ser TCA	wt with all Ser tca	wt with all Ser tca	onc
IgkS2-38	Ser TCT	wt with all Ser tct	wt with all Ser tct	onc
IgkS2-39	Ser TCC	wt	wt with all Ser tcc	onc
IgkS2-40	Thr ACG	wt with all Thr acg	wt with all Thr acg	onc
IgkS2-41	Thr ACA	wt with all Thr aca	wt with all Thr aca	onc
IgkS2-42	Thr ACT	wt with all Thr act	wt with all Thr act	onc
IgkS2-43	Thr ACC	wt with all Thr acc	wt with all Thr acc	onc
IgkS2-44	Tyr TAT	mc	mc	linkerY-onc
IgkS2-45	Tyr TAC	mc	mc	linkerY-onc
IgkS2-46	Val GTG	wt with all Val gtg	wt with all Val gtg	onc
IgkS2-47	Val GTA	wt with all Val gta	wt with all Val gta	onc
IgkS2-48	Val GTT	wt with all Val gtt	wt with all Val gtt	onc
IgkS2-49	Val GTC	wt with all Val gtc	wt with all Val gtc	onc
IgkS2-	Asn AAT	wt	wt with all Asn	linkerN-non-onc

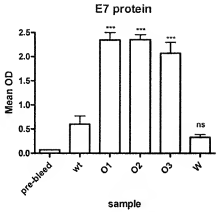
Construct	Amino acid & Codon	Codon usage of Secretory Sequence	Codon usage of E7	E7 Protein
11b IgkS2-12b	Asn AAC	wt	aat wt with all Asn aac	linkerN-non-onc

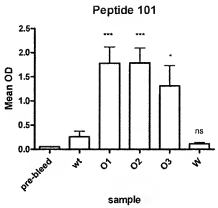
APPENDIX C

Amino Acid	Ranking of Immune Response Preferences for Synonymous Codons
Ala	$Ala^{GCT} > Ala^{GCC} > (Ala^{GCA}, Ala^{GCG})$
Arg	$(Arg^{CGA}, Arg^{CGC}, Arg^{CGT}, Arg^{AGA}) > (Arg^{AGG}, Arg^{CGG})$
Asn	$Asn^{AAC} > Asn^{AAT}$
Asp	$Asp^{GAC} > Asp^{GAT}$
Cys	$Cys^{TGC} > Cys^{TGT}$
Glu	$Glu^{GAA} > Glu^{GAG}$
Gln	$Gln^{CAA} = Gln^{CAG}$
Gly	$Gly^{GGA} > (Gly^{GGG}, Gly^{GGT}, Gly^{GGC})$
His	$His^{CAC} = His^{CAT}$
Ile	$Ile^{ATC} >> Ile^{ATT} > Ile^{ATA}$
Leu	$(Leu^{CTG}, Leu^{CTC}) > (Leu^{CTA}, Leu^{CTT}) >> Leu^{TTG} > Leu^{TTA}$
Lys	$Lys^{AAG} = Lys^{AAA}$
Phe	$Phe^{TTT} > Phe^{TTC}$
Pro	$Pro^{CCC} > Pro^{CCT} >> (Pro^{CCA}, Pro^{CCG})$
Ser	$Ser^{TCG} >> (Ser^{TCT}, Ser^{TCA}, Ser^{TCC}) >> (Ser^{AGC}, Ser^{AGT})$
Thr	$Thr^{ACG} > Thr^{ACC} >> Thr^{ACA} > Thr^{ACT}$
Tyr	$Tyr^{TAC} > Tyr^{TAT}$
Val	$(Val^{GTG}, Val^{GTC}) > Val^{GTT} > Val^{GTA}$

APPENDIX D

Antibody response





Cellular response